

What is claimed is:

1. A Vitaxin antibody exhibiting selective binding affinity to $\alpha_v\beta_3$ comprising at least one Vitaxin heavy chain polypeptide comprising substantially the same variable region amino acid sequence as that shown in Figure 1A (SEQ ID NO:2) and at least one Vitaxin light chain polypeptide comprising substantially the same variable region amino acid sequence as that shown in Figure 1B (SEQ ID NO:4) or a functional fragment thereof.
- 10 2. The Vitaxin antibody of claim 1, wherein said functional fragment is selected from the group consisting of Fv, Fab, F(ab)₂ and scFV.
- 15 3. A nucleic acid encoding a Vitaxin heavy chain polypeptide comprising substantially the same Vitaxin heavy chain variable region nucleotide sequences as that shown in Figure 1A (SEQ ID NO:1) or a fragment thereof.
- 20 4. The nucleic acid of claim 3, wherein said fragment further comprises a nucleic acid encoding substantially the same nucleotide sequence as the variable region of said Vitaxin heavy chain polypeptide (SEQ ID NO:1).
- 25 5. The nucleic acid of claim 3, wherein said fragment further comprises a nucleic acid encoding substantially the same nucleotide sequence as a CDR of said Vitaxin heavy chain polypeptide.

6. A nucleic acid encoding a Vitaxin light chain polypeptide comprising substantially the same Vitaxin light chain variable region nucleotide sequences as that shown in Figure 1B (SEQ ID NO:3) or a fragment thereof.

7. The nucleic acid of claim 6, wherein said fragment further comprises a nucleic acid encoding substantially the same nucleotide sequence as the variable region of said Vitaxin light chain polypeptide (SEQ ID NO:3).

8. The nucleic acid of claim 6, wherein said fragment further comprises a nucleic acid encoding substantially the same nucleotide sequence as a CDR of said Vitaxin light chain polypeptide.

9. A nucleic acid encoding a Vitaxin heavy chain polypeptide comprising a nucleotide sequence encoding substantially the same Vitaxin heavy chain variable region amino acid sequence as that shown in Figure 1A (SEQ ID NO:2) or fragment thereof.

10. The nucleic acid of claim 9, wherein said fragment further comprises a nucleic acid encoding substantially the same heavy chain variable region amino acid sequence of said Vitaxin heavy chain amino acid sequence (SEQ ID NO:2).

11. The nucleic acid of claim 9, wherein said fragment further comprises a nucleic acid encoding substantially the same heavy chain CDR amino acid sequence of said Vitaxin heavy chain amino acid sequence.

12. A nucleic acid encoding a Vitaxin light chain polypeptide comprising a nucleotide sequence encoding substantially the same Vitaxin light chain variable region amino acid sequence as that shown in
5 Figure 1B (SEQ ID NO:4) or fragment thereof.

13. The nucleic acid of claim 12, wherein said fragment further comprises a nucleic acid encoding substantially the same light chain variable region amino acid sequence of said Vitaxin light chain amino acid
10 sequence (SEQ ID NO:4).

14. The nucleic acid of claim 12, wherein said fragment further comprises a nucleic acid encoding substantially the same light chain CDR amino acid sequence of said Vitaxin light chain amino acid sequence.

15. A Vitaxin heavy chain polypeptide comprising substantially the same variable region amino acid sequence as that shown in Figure 1A (SEQ ID NO:2) or functional fragment thereof.

16. The Vitaxin heavy chain polypeptide of
20 claim 15, wherein said functional fragment comprises a variable chain polypeptide or a CDR polypeptide.

17. A Vitaxin light chain polypeptide comprising substantially the same variable region amino acid sequence as that shown in Figure 1B (SEQ ID NO:4) or
25 a functional fragment thereof.

18. The Vitaxin light chain polypeptide of
claim 17, wherein said functional fragment comprises a variable chain polypeptide or a CDR polypeptide.

19. A LM609 grafted antibody exhibiting selective binding affinity to $\alpha_v\beta_3$ comprising at least one LM609 grafted heavy chain polypeptide comprising substantially the same variable region amino acid sequence as that shown in Figure 1A (SEQ ID NO:2) and at least one LM609 grafted light chain polypeptide comprising substantially the same variable region amino acid sequence as that shown in Figure 7 (SEQ ID NO:32) or a functional fragment thereof.

10 20. The LM609 grafted antibody of claim 19, wherein said functional fragment is selected from the group consisting of Fv, Fab, F(ab)₂ and scFV.

15 21. A nucleic acid encoding a LM609 grafted heavy chain polypeptide comprising substantially the same LM609 grafted heavy chain variable region nucleotide sequences as that shown in Figure 1A (SEQ ID NO:1) or a fragment thereof.

20 22. The nucleic acid of claim 21, wherein said fragment further comprises a nucleic acid encoding substantially the same nucleotide sequence as the variable region of said LM609 grafted heavy chain polypeptide (SEQ ID NO:1).

25 23. The nucleic acid of claim 21, wherein said fragment further comprises a nucleic acid encoding substantially the same nucleotide sequence as a CDR of said LM609 grafted heavy chain polypeptide.

24. A nucleic acid encoding a LM609 grafted light chain polypeptide comprising substantially the same LM609 grafted light chain variable region nucleotide sequences as that shown in Figure 7 (SEQ ID NO:31) or a 5 fragment thereof.

25. The nucleic acid of claim 24, wherein said fragment further comprises a nucleic acid encoding substantially the same nucleotide sequence as the variable region of said LM609 grafted light chain 10 polypeptide (SEQ ID NO:31).

26. The nucleic acid of claim 24, wherein said fragment further comprises a nucleic acid encoding substantially the same nucleotide sequence as a CDR of said LM609 grafted light chain polypeptide.

15 27. A nucleic acid encoding a LM609 grafted antibody heavy chain polypeptide comprising a nucleotide sequence encoding substantially the same LM609 grafted heavy chain variable region amino acid sequence as that shown in Figure 1A (SEQ ID NO:2) or fragment thereof.

20 28. The nucleic acid of claim 27, wherein said fragment further comprises a nucleic acid encoding substantially the same heavy chain variable region amino acid sequence of said LM609 grafted heavy chain amino acid sequence (SEQ ID NO:2).

25 29. The nucleic acid of claim 27, wherein said fragment further comprises a nucleic acid encoding substantially the same heavy chain CDR amino acid sequence of said LM609 grafted heavy chain amino acid sequence.

30. A nucleic acid encoding a LM609 grafted antibody light chain polypeptide comprising a nucleotide sequence encoding substantially the same LM609 grafted light chain variable region amino acid sequence as that shown in Figure 7 (SEQ ID NO:32) or fragment thereof.

31. The nucleic acid of claim 30, wherein said fragment further comprises a nucleic acid encoding substantially the same light chain variable region amino acid sequence of said Vitaxin light chain amino acid sequence (SEQ ID NO:32).

32. The nucleic acid of claim 30, wherein said fragment further comprises a nucleic acid encoding substantially the same light chain CDR amino acid sequence of said Vitaxin light chain amino acid sequence.

33. A LM609 grafted heavy chain polypeptide comprising substantially the same variable region amino acid sequence as that shown in Figure 1A (SEQ ID NO:2) or functional fragment thereof.

34. The LM609 grafted heavy chain polypeptide of claim 33, wherein said functional fragment comprises a variable chain polypeptide or a CDR polypeptide.

35. A LM609 grafted light chain polypeptide comprising substantially the same variable region amino acid sequence as that shown in Figure 7 (SEQ ID NO:32) or a functional fragment thereof.

36. The LM609 grafted light chain polypeptide of claim 35, wherein said functional fragment comprises a variable chain polypeptide or a CDR polypeptide.

37. A nucleic acid encoding a heavy chain polypeptide for monoclonal antibody LM609 comprising substantially the same heavy chain variable region nucleotide sequence as that shown in Figure 2A (SEQ ID NO:5) or a fragment thereof.

38. The nucleic acid of claim 37, wherein said fragment further comprises a nucleic acid encoding substantially the same nucleotide sequence as the variable region of said heavy chain polypeptide (SEQ ID NO:5).

39. The nucleic acid of claim 37, wherein said fragment further comprises a nucleic acid encoding substantially the same nucleotide sequence as a CDR of said heavy chain polypeptide.

40. A nucleic acid encoding a light chain polypeptide for monoclonal antibody LM609 comprising substantially the same light chain variable region nucleotide sequence as that shown in Figure 2B (SEQ ID NO:7) or a fragment thereof.

41. The nucleic acid of claim 40, wherein said fragment further comprises a nucleic acid encoding substantially the same nucleotide sequence as the variable region of said light chain polypeptide (SEQ ID NO:7).

42. The nucleic acid of claim 40, wherein said fragment further comprises a nucleic acid encoding substantially the same nucleotide sequence as a CDR of said light chain polypeptide.

43. A nucleic acid encoding a heavy chain polypeptide for monoclonal antibody LM609 comprising a nucleotide sequence encoding substantially the same heavy chain variable domain amino acid sequence of monoclonal antibody LM609 as that shown in Figure 2A (SEQ ID NO:6) or fragment thereof.

44. The nucleic acid of claim 43, wherein said fragment further comprises a nucleic acid encoding substantially the same heavy chain variable region amino acid sequence of said monoclonal antibody LM609 (SEQ ID NO:6).

45. The nucleic acid of claim 43, wherein said fragment further comprises a nucleic acid encoding substantially the same heavy chain CDR amino acid sequence as said monoclonal antibody LM609.

46. A nucleic acid encoding a heavy chain polypeptide for monoclonal antibody LM609 comprising a nucleotide sequence encoding substantially the same light chain amino acid sequence of monoclonal antibody LM609 as that shown in Figure 2B (SEQ ID NO:8) or fragment thereof.

47. The nucleic acid of claim 46, wherein said fragment further comprises a nucleic acid encoding substantially the same light chain variable region amino acid sequence of said monoclonal antibody LM609 (SEQ ID NO:8).

48. The nucleic acid of claim 46, wherein said fragment further comprises a nucleic acid encoding substantially the same light chain CDR amino acid sequence as said monoclonal antibody LM609.

49. A method of inhibiting a function of $\alpha_v\beta_3$, comprising contacting $\alpha_v\beta_3$ with Vitaxin or a functional fragment thereof under conditions which allow binding of Vitaxin to $\alpha_v\beta_3$.

5 50. The method of claim 49, wherein said functional fragment is selected from the group consisting of Fv, Fab, $F(ab)_2$ and scFV.

51. The method of claim 49, wherein said function of $\alpha_v\beta_3$ is binding of $\alpha_v\beta_3$ to a ligand.

10 52. The method of claim 49, wherein said function of $\alpha_v\beta_3$ is integrin mediated signal transduction.

15 53. A method of treating an $\alpha_v\beta_3$ -mediated disease comprising administering an effective amount of Vitaxin or a functional fragment thereof under conditions which allow binding to $\alpha_v\beta_3$.

54. The method of claim 53, wherein said functional fragment is selected from the group consisting of Fv, Fab, $F(ab)_2$ and scFV.

20 55. The method of claim 53, wherein said $\alpha_v\beta_3$ -mediated disease is angiogenesis or restenosis.

25 56. An enhanced LM609 grafted antibody exhibiting selective binding affinity to $\alpha_v\beta_3$, or a functional fragment thereof, comprising at least one amino acid substitution in one or more CDRs of a LM609 grafted heavy chain variable region polypeptide or a LM609 grafted light chain variable region polypeptide, wherein the $\alpha_v\beta_3$ binding affinity of said enhanced LM609 grafted antibody is maintained.

57. The enhanced LM609 grafted antibody of claim 56, wherein said $\alpha_v\beta_3$ binding affinity of said LM609 grafted antibody is enhanced.

58. The enhanced LM609 grafted antibody of
5 claim 56, wherein said functional fragment is selected from the group consisting of Fv, Fab, F(ab)₂ and scFV.

59. The enhanced LM609 grafted antibody of
claim 56, wherein said CDR having at least one amino acid substitution is selected from the group consisting of
10 V_H CDR1, V_H CDR2, V_H CDR3, V_L CDR1, V_L CDR2 and V_L CDR3.

60. The enhanced LM609 grafted antibody of
claim 59, wherein said V_H CDR1 is selected from the group consisting of the CDRs referenced as SEQ ID NO:48, SEQ ID NO:50 and SEQ ID NO:52.

15 61. The enhanced LM609 grafted antibody of
claim 59, wherein said V_H CDR2 is selected from the group consisting of the CDRs referenced as SEQ ID NO:54, SEQ ID NO:56 and SEQ ID NO:58.

20 62. The enhanced LM609 grafted antibody of
claim 59, wherein said V_H CDR3 is selected from the group consisting of the CDRs referenced as SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:94, SEQ ID NO:96; SEQ ID NO:98 and SEQ ID NO:100.

25 63. The enhanced LM609 grafted antibody of
claim 59, wherein said V_L CDR1 is the CDR referenced as SEQ ID NO:82.

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64. The enhanced LM609 grafted antibody of
claim 59, wherein said V_L CDR2 is the CDR referenced as
SEQ ID NO:84.

65. The enhanced LM609 grafted antibody of
5 claim 59, wherein said V_L CDR3 is selected from the group
consisting of the CDRs referenced as SEQ ID NO:86, SEQ ID
NO:88, SEQ ID NO:90 and SEQ ID NO:92.

66. The enhanced LM609 grafted antibody of
claim 56, wherein said enhanced LM609 grafted antibody
10 comprises at least one amino acid substitution in two or
more CDRs of a LM609 grafted heavy chain variable region
polypeptide or a LM609 grafted light chain variable
region polypeptide.

67. The enhanced LM609 grafted antibody of
15 claims 66, wherein said functional fragment is selected
from the group consisting of Fv, Fab, F(ab)₂ and scFV.

68. The enhanced LM609 grafted antibody of
claim 66, wherein said CDR having at least one amino acid
substitution is selected from the group consisting of V_H
20 CDR1, V_H CDR2, V_H CDR3, V_L CDR1, V_L CDR2 and V_L CDR3.

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69. The enhanced LM609 grafted antibody of claim 68, wherein said enhanced LM609 grafted antibody comprises the combination of CDRs selected from the group consisting of:

5 the V_L CDR1 referenced as SEQ ID NO:82 and the V_H CDR3 referenced as SEQ ID NO:68;

 the V_L CDR1 referenced as SEQ ID NO:82, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:68;

10 the V_L CDR1 referenced as SEQ ID NO:82, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:72;

 the V_L CDR1 referenced as SEQ ID NO:82, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:70;

 the V_L CDR1 referenced as SEQ ID NO:82 and the V_H CDR3 referenced as SEQ ID NO:72;

 the V_L CDR3 referenced as SEQ ID NO:86, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:68;

 the V_L CDR3 referenced as SEQ ID NO:90 and V_H CDR3 referenced as SEQ ID NO:68; and

 the V_L CDR3 referenced as SEQ ID NO:90, the V_H CDR2 referenced as SEQ ID NO:56 and V_H CDR3 referenced as SEQ ID NO:68.

70. The enhanced LM609 grafted antibody of claim 66, wherein at least one of said CDRs has two or more amino acid substitutions.

71. The enhanced LM609 grafted antibody of claims 70, wherein said functional fragment is selected from the group consisting of Fv, Fab, F(ab)₂ and scFV.

72. The enhanced LM609 grafted antibody of claim 70, wherein said CDR having at least one amino acid substitution is selected from the group consisting of V_H CDR1, V_H CDR2, V_H CDR3, V_L CDR1, V_L CDR2 and V_L CDR3.

5 73. The enhanced LM609 grafted antibody of claim 72, wherein said enhanced LM609 grafted antibody comprises the combination of CDRs selected from the group consisting of:

10 the V_L CDR1 referenced as SEQ ID NO:82, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:94;

15 the V_L CDR3 referenced as SEQ ID NO:90, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:94;

20 the V_L CDR3 referenced as SEQ ID NO:90, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:96;

25 the V_L CDR3 referenced as SEQ ID NO:90 and the V_H CDR3 referenced as SEQ ID NO:94;

30 the V_L CDR3 referenced as SEQ ID NO:90 and the V_H CDR3 referenced as SEQ ID NO:98; and

 the V_L CDR3 referenced as SEQ ID NO:90, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:100.

25 74. A high affinity LM609 grafted antibody exhibiting selective binding affinity to $\alpha_v\beta_3$, or a functional fragment thereof, comprising at least one amino acid substitution in one or more CDRs of a LM609 grafted heavy chain variable region polypeptide or a LM609 grafted light chain variable region polypeptide, wherein the $\alpha_v\beta_3$ binding affinity of said high affinity LM609 grafted antibody is enhanced.

75. The high affinity LM609 grafted antibody of claim 74, wherein said functional fragment is selected from the group consisting of Fv, Fab, F(ab)₂ and scFV.

76. The high affinity LM609 grafted antibody of claim 74, wherein said CDR having at least one amino acid substitution is selected from the group consisting of V_H CDR1, V_H CDR2, V_H CDR3, V_L CDR1, V_L CDR2 and V_L CDR3.

77. The high affinity LM609 grafted antibody of claim 76, wherein said high affinity LM609 grafted antibody comprises the combination of CDRs selected from the group consisting of:

the V_L CDR1 referenced as SEQ ID NO:82 and the V_H CDR3 referenced as SEQ ID NO:68;

the V_L CDR1 referenced as SEQ ID NO:82, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:68;

the V_L CDR1 referenced as SEQ ID NO:82, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:72;

the V_L CDR1 referenced as SEQ ID NO:82, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:70;

the V_L CDR1 referenced as SEQ ID NO:82 and the V_H CDR3 referenced as SEQ ID NO:72;

the V_L CDR3 referenced as SEQ ID NO:86, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:68;

the V_L CDR3 referenced as SEQ ID NO:90, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:94;

the V_L CDR3 referenced as SEQ ID NO:90 and V_H CDR3 referenced as SEQ ID NO:68;

the V_L CDR3 referenced as SEQ ID NO:90, the V_H CDR2 referenced as SEQ ID NO:56 and V_H CDR3 referenced as SEQ ID NO:68;

5 the V_L CDR1 referenced as SEQ ID NO:82, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:94;

the V_L CDR3 referenced as SEQ ID NO:90, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:96;

10 the V_L CDR3 referenced as SEQ ID NO:90 and the V_H CDR3 referenced as SEQ ID NO:94;

the V_L CDR3 referenced as SEQ ID NO:90 and the V_H CDR3 referenced as SEQ ID NO:98; and

15 the V_L CDR3 referenced as SEQ ID NO:90, the V_H CDR2 referenced as SEQ ID NO:56 and the V_H CDR3 referenced as SEQ ID NO:100.

78. A nucleic acid encoding an enhanced LM609 grafted antibody, or a functional fragment thereof, exhibiting selective binding affinity to $\alpha_v\beta_3$ comprising 20 at least one amino acid substitution in one or more CDRs of a LM609 grafted heavy chain variable region polypeptide or a LM609 grafted light chain variable region polypeptide, wherein the $\alpha_v\beta_3$ binding affinity of said enhanced LM609 grafted antibody is maintained or 25 enhanced.

79. A nucleic acid encoding a high affinity LM609 grafted antibody, or a functional fragment thereof, exhibiting selective binding affinity to $\alpha_v\beta_3$ comprising 30 at least one amino acid substitution in one or more CDRs of a LM609 grafted heavy chain variable region polypeptide or a LM609 grafted light chain variable region polypeptide, wherein the $\alpha_v\beta_3$ binding affinity of said high affinity LM609 grafted antibody is enhanced.